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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/779,439 | 02/08/2001 | Antoine Noujaim | 107823.178 | 6671 |

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| EXAMINER |
|---|
| HELMS, LARRY RONALD |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | 12 |

DATE MAILED: 09/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/779,439 | Applicant(s) NOUJAIM, ANTOINE | |
|---|---|---|---|
| | Examiner Larry R. Helms | Art Unit 1642 | |

*-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *27 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of Group X, claims 22-25 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in Paper No. 10.

3. Claims 22-25 are under examination.

4. NOTE: The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

| Mailroom Stamp Date | Certificate of Mailing Date |
|---|---|
| 6/27/02 | 6/21/02 |
| | |
| | |
| | |

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

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If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the

Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.

***Information Disclosure Statement***

5. The information disclosure statement filed 7/1/02 has been considured, however, reference A6 lacks a full citation. There is no volume, page, or year. If applicant would supply this information the examiner will add this to the IDS, otherwise if this application goes on to issue this reference will not be included on the face of the patent.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 22-25 are indefinite for reciting 'diagnosing the efficacy" in claim 22 because the exact meaning of the phrase is not clear. The phrase "diagnosing the efficacy" is indefinite when the claims fail to state the function which is to be achieved. The specification defines "diagnosing the efficacy" as "predicting the time after administration of a xenotypic antibody at which relapse occurs" (see page 5, lines 25-

25). It is unclear what "relapse" is contemplated. Does the phrase mean relapse of a disease in which the antigen that the xenotypic antibody binds or another disease not associated with the antigen or increase in antigen to which the xenotypic antibody binds in the body or the time at which adding more of the xenotypic antibody has no effect on the disease, or some other meaning? In addition, if the definition on page 5 is used, then the method seemingly requires a patient that has a disease associated with the antigen to which the antibody binds, otherwise how can one have a relapse, however, the claim does not recite this and this is indefinite. In addition, it is unclear how one "predicts" the time at which "relapse" occurs.

b. Claims 22-25 are indefinite for reciting "favorable diagnosis" because the exact meaning of the phrase is not clear. The phrase "favorable diagnosis" is defined in the specification as "a diagnosis that predicts that the time after administration of a xenotypic antibody at which relapse occurs is longer than the time after administration of a placebo at which relapse occurs" (see page 5-6 bridging paragraph). The claims are indefinite because it is unclear whether to diagnose the patent has to be given a placebo and if so essential method steps have been left out of the method.

c. Claim 24 recites the limitation "T helper cell response" in claim 22. There is insufficient antecedent basis for this limitation in the claim.

***Claim R j ctions - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al (WO 97/42973, published 11/20/97, IDS #5) and further in view of Goletz et al (U.S. Patent 5,997,869, issued 12/99).

The claims recite a method for diagnosing the efficacy of xenotypic antibody-mediated immunotherapy comprising measuring the level of a T helper cell or cytotoxic T cell response in a human to a target antigen of the xenotypic antibody after administration of the antibody to the patient, wherein an increase in the level of the T cell response produced after administration of the antibody relative to the level produced by the patient prior to administration is indicative of a favorable diagnosis of efficacy. Due to the indefinite nature of the claims (see 112 second above) the claims are being interpreted to mean a method of determining if a T cell response was

generated after xenotypic antibody administration and if there is an increased survival of the patients when the xenotypic antibody is administered to the patient.

Madiyalakan et al teach administration of a mouse antibody directed to CA125 which is Mab-B43.13 which led to increased in cytotoxic T lymphocytes in human cancer patients (see Examples 2 and 8) and stimulates both a humoral and cellular response and administration of the xenotypic antibody led to an increase in the mean survival of the patients (see example 9). Madiyalakan et al does not specifically teach measuring the T cell response prior to administration of the antibody. This deficiency is made up for in the teachings of Goletz et al.

Goletz et al teach methods to immunize humans to induce cytotoxic T lymphocytes. Goletz et al also teach as a preliminary step to determine the T cell response prior to administration of an agent (see column 15, lines 41-44).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have determined the T cell response prior to administration of the xenotypic antibody as taught by Goletz et al and add this to the method of Madiyalakan et al which teaches measuring the T cell response after administration of the xenotypic antibody.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody as taught by Goletz et al and add this to the method of Madiyalakan et al which teaches measuring the T cell response after administration of the xenotypic antibody because Goletz et al teach that a preliminary

step can be performed to determine the CTL response prior to immunization. In addition one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody as taught by Goletz et al and add this to the method of Madiyalakan et al which teaches measuring the T cell response after administration of the xenotypic antibody because Madiyalakan et al teach a method for stimulating a cytotoxic T cell response and after administration of the xenotypic antibody a CTL response was generated (see example 9). Thus, it would have been obvious to one skill in the art to determine the CTL response prior to administration because it is routine in the art to perform such a determination of CTL response prior to immunization in order to have a control to determine if an enhanced CTL response was obtained.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

10. Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al (U.S. Patent 6,241,985, filed 3/20/98, IDS #5) and further in view of Goletz et al (U.S. Patent 5,997,869, issued 12/99).

The claims and the interpretation of the claims have been described supra.

Madiyalakan et al teach administration of a mouse antibody directed to CA125 which is Mab-B43.13 which led to increased in cytotoxic T lymphocytes in human cancer patients (see Examples 2 and 8) and stimulates both a humoral and cellular response and administration of the xenotypic antibody led to an increase in the mean

survival of the patients (see example 9). Madiyalakan et al does not specifically teach measuring the T cell response prior to administration of the antibody. This deficiency is made up for in the teachings of Goletz et al.

Goletz et al teach methods to immunize humans to induce cytotoxic T lymphocytes and assays for determination of T cell responses. Goletz et al also teach as a preliminary step to determine the T cell response prior to administration of an agent (see column 15, lines 41-44).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have determined the T cell response prior to administration of the xenotypic antibody as taught by Goletz et al and add this to the method of Madiyalakan et al which teaches measuring the T cell response after administration of the xenotypic antibody.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody as taught by Goletz et al and add this to the method of Madiyalakan et al which teaches measuring the T cell response after administration of the xenotypic antibody because Goletz et al teach that a preliminary step can be performed to determine the CTL response prior to immunization. In addition one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have determined the T cell response prior to administration of the xenotypic antibody as taught by Goletz et al and add this to the method of Madiyalakan et al which teaches measuring the T cell response after

administration of the xenotypic antibody because Madiyalakan et al teach a method for stimulating a cytotoxic T cell response and after administration of the xenotypic antibody a CTL response was generated (see example 9). Thus, it would have been obvious to one skill in the art to determine the CTL response prior to administration because it is routine in the art to perform such a determination of CTL response prior to immunization in order to have a control to determine if an enhanced CTL response was obtained.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

***Conclusion***

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879